

We claim:

1. A particulate composition for drug delivery to the pulmonary system comprising:

biodegradable particles incorporating a therapeutic agent and a material selected from the group consisting of surfactant and a molecule having a charge opposite to the charge of the therapeutic agent and forming a complex thereto, wherein the particles have a tap density less than 0.4 g/cm^3 and a mean diameter between $5 \text{ }\mu\text{m}$ and $30 \text{ }\mu\text{m}$ effective to yield an aerodynamic diameter of the particles of between approximately one and five microns.

2. The composition of claim 1 wherein the aerodynamic diameter of the particles is between approximately one and three microns.

3. The composition of claim 1 wherein at least 50% of the particles have a mean diameter between $5 \text{ }\mu\text{m}$ and $15 \text{ }\mu\text{m}$ and a tap density less than 0.1 g/cm^3 .

4. The composition of claim 1 further comprising a pharmaceutically acceptable carrier for administration to the lungs.

5. The composition of claim 1 wherein the particles comprise a biodegradable polymer.

6. The composition of claim 1 wherein the particles comprise a complex of charged molecules and a surfactant.

7. The composition of claim 1 wherein the particles comprise an excipient.

8. The composition of claim 1 wherein the particles have an irregular surface structure.

9. The composition of claim 1 wherein the surfactant is coated on the surface of the particle.

10. The composition of claim 1 wherein the surfactant is incorporated within and on the surface of the particle.

11. The composition of claim 1 wherein the therapeutic agent is selected from the group consisting of proteins, polysaccharides, lipids, nucleic acids and combinations thereof.

7-12. The composition of claim 1 wherein the therapeutic agent is selected from the group consisting of nucleotides and oligonucleotides.

8-13. The composition of claim 1 wherein the therapeutic agent is selected from the group consisting of insulin, calcitonin, leuprolide and albuterol.

9-14. The composition of claim 1 wherein the surfactant is selected from the group consisting of a fatty acid, a phospholipid, and a block copolymer.

10-15. The composition of claim 1 wherein the surfactant is a phosphoglyceride.

11-16. The composition of claim 1 wherein the surfactant is L- α -phosphatidylcholine dipalmitoyl.

12-17. The composition of claim 1 wherein the agent is a charged species and is present as a complex with an oppositely charged species.

13-18. The composition of claim 1 wherein the agent is hydrophilic and is present as a complex with a hydrophobic moiety.

14-19. A method for drug delivery to the pulmonary system comprising:

administering to the respiratory tract of a patient in need of treatment an effective amount of biodegradable particles incorporating a therapeutic agent and a molecule selected from the group consisting of surfactant and a molecule having a charge opposite to the charge of the therapeutic agent and forming a complex thereto,

wherein the particles have a tap density less than about 0.4 g/cm³ and a mean diameter of between 5 μ m and 30 μ m effective to yield an aerodynamic diameter of the particles of between approximately one and five microns.

15-20. The method of claim 19 wherein the aerodynamic diameter of the particles is between approximately one and three microns.

16-21. The method of claim 19 wherein at least 50% of the administered particles have a mean diameter between 5 μ m and 15 μ m.

1722. The method of claim 19 wherein at least 50% of the administered particles have a mean diameter between 5 μm and 15 μm and a tap density of less than about 0.1 g/cm³.

23. The method of claim 19 wherein the particles comprise a biodegradable polymer.

1824. The method of claim 19 wherein the particles comprise a complex of charged molecules and surfactant.

25. The method of claim 19 wherein the particles comprise an excipient.

26. The method of claim 23 wherein the particles have an irregular surface structure and have surfactant incorporated on or within the particle.

1927. The method of claim 19 for delivery to the alveolar zone of the lung wherein at least 90% of the particles have a mean diameter between about 9 μm and 11 μm and a tap density less than 0.1 g/cm³.

2028. The method of claim 19 wherein the therapeutic agent is selected from the group consisting of proteins, polysaccharides, lipids, nucleic acids and combinations thereof.

2129. The method of claim 19 wherein the therapeutic agent selected from the group consisting of nucleotides and oligonucleotides.

2230. The method of claim 28 wherein the therapeutic agent is selected from the group consisting of insulin, calcitonin, leuprolide and albuterol.

31. The method of claim 19 wherein the particles are administered in combination with a pharmaceutically acceptable carrier for administration to the respiratory tract.

2332. The method of claim 19 wherein the surfactant is selected from the group consisting of a fatty acid, a phospholipid, and a block copolymer.

2433. The method of claim 32 wherein the surfactant is a phosphoglyceride.

25 34. The method of claim 32 wherein the surfactant is L- α -phosphatidylcholine dipalmitoyl.

35. The method of claim 32 wherein the surfactant is coated on the surface of the particle.

36. The method of claim 32 wherein the surfactant is incorporated within and on the surface of the particle.

20 37. The method of claim 19 wherein the agent is a charged species and is present as a complex with an oppositely charged species.

21 38. The method of claim 19 wherein the agent is hydrophilic and is present as a complex with a hydrophobic moiety.

08971791 44763